EXHIBIT A

Attorney Docket No.: 9050-0048.20 Mailing Date: May 15, 2003

Inventor(s): Peter Tam et al.

Serial No.: 09/996,407 Filing Date: November 21, 2001

Document(s):

Transmittal Form (dupl);
Fee Transmittal;
Amendment under 37 CFR § 1.111;
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TRANSMITTAL FORM

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Total Number of Pages in This Submission: 21

Application Number	09/996,407
Filing Date	November 21, 2001
First Named Inventor	Peter Tam
Art Unit	1615
Examiner Name	Carlos A. AZPURU
Attorney Docket Number	9050-0048.20

ENCLOSURES (Check all that apply)

- ☒ **No Fee Due**
  - ☒ **Fee Transmittal**
- ☐ Fee(s) Due
  - ☐ Fee Transmittal (+ copy)
  - ☐ Check for $*
- ☒ **Charge any underpayment or credit any overpayment to Deposit Account No. 18-0580**
- ☒ **Amendment/Reply**
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  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement & Form(s) PTO-1449
  - ☐ Copy(ies) of cited reference(s)
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts / Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation, Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s):
- ☐ After Allowance Communication to a Technology Center (TC)
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- ☐ Proprietary Information
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- ☐ Other Enclosure(s) (please identify below):

Remarks:

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Name (print/type)	Shelley P. Eberle	Registration No. (Attorney/Agent)	31,411	Telephone	(650) 330-0900
Signature	Shelley P. Eberle			Date	May 15, 2003

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Non Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on May 15, 2003.

Name (print/type)	Joe Clark		
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FEE TRANSMITTAL for FY 2003

Effective 01/01/03. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT | $0.00

Complete if Known	
Application Number	09/996,407
Filing Date	November 21, 2001
First Named Inventor	Peter Tam
Examiner Name	Carlos A. AZPURU
Group Art Unit	1615
Attorney Docket No.	9050-0048.20

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☒ None

☐ Deposit Account:

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Deposit Account Name	

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☐ Charge fee(s) indicated below ☐ Charge any underpayment or credit any overpayments

☐ Charge any additional fee(s) during the pendency of this application

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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1) $

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims		Fee from below		Fee Paid
Total Claims	71	- 75** =	0	x		=	
Independent Claims	3	- 3** =	0	x		=	
Multiple Dependent						=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claim in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) $0

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for ex *parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive – unavoidable	
1453	1,300	2453	650	Petition to revive – unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid **SUBTOTAL (3)** $

SUBMITTED BY				Complete *(if applicable)*	
Name (Print/Type)	Shelley P. Eberle	*Registration No. (Attorney/Agent)*	31,411	*Telephone*	(650) 330-0900
Signature	Shelley P. Eberle			*Date*	May 15, 2003

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:
Peter TAM et al.

Confirmation No.: 3091

Serial No.: 09/996,407

Group Art Unit: 1614

Filing Date: November 21, 2001

Examiner: Carlos A. AZPURU

Title: AS-NEEDED ADMINISTRATION OF TRICYCLIC AND OTHER NON-SRI ANTIDEPRESSANT DRUGS TO TREAT PREMATURE EJACULATION

AMENDMENT UNDER 37 CFR § 1.111

Mail Stop Non Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is in response to the Office Action mailed March 21, 2003. ***As this response is being filed within the three-month shortened statutory period set for response, no extension of time is necessary.*** Applicants respectfully request entry of the following amendments and reconsideration of the application in light of the following amendments and remarks as follows:

Amendments to the Claims are reflected in the listing of the claims which begins on page 2 of this document.

Remarks begin on page 12 of this document.

This listing of the claims will replace all prior versions, and listings, of claims in the application:

LISTING OF THE CLAIMS

Claim 1 (Currently amended). A method for treating premature ejaculation, which comprises systemically administering to a male individual in need of such treatment, [on an as-needed basis] less than 3.5 hours prior to anticipated sexual activity, a rapid-release pharmaceutical formulation containing a therapeutically effective amount of an antidepressant drug selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressants, monoamine oxidase inhibitors, azaspirone antidepressants, and atypical non-SRI antidepressants, wherein the formulation releases the drug at a rate that provides a systemically effective level of the drug within 3.5 hours of administration.

Claim 2 (Original). The method of claim 1, wherein the antidepressant drug is contained within a pharmaceutical formulation.

Claim 3 (Original). The method of claim 2, wherein the pharmaceutical formulation is a unit dosage form.

Claim 4 (Currently amended). The method of claim 2 [3], wherein the antidepressant drug is administered immediately prior to anticipated sexual activity.

Claim 5 (Currently amended). The method of claim 1 [4], wherein the antidepressant drug is administered about 0.25 to about 3.5 hours prior to anticipated sexual activity.

Claim 6 (Currently amended). The method of claim 5, wherein the [active agent] antidepressant drug is administered about 0.5 to about 3.0 hours prior to anticipated sexual activity.

Claim 7 (Currently amended). The method of claim 6, wherein the [active agent] antidepressant drug is administered about 1 to about 2.5 hours prior to anticipated sexual activity.

Claim 8 (Original). The method of any one of claims 4, 5, 6 and 7, wherein the sexual activity is sexual intercourse.

Claim 9 (Original). The method of claim 2, wherein the formulation is an immediate release dosage form.

Claim 10 (Original). The method of claim 3, wherein the formulation is an immediate release unit dosage form.

Claim 11 (Currently amended). The method of claim [1] 2, wherein the [active agent] pharmaceutical formulation is administered orally.

Claim 12 (Original). The method of claim 11, wherein the pharmaceutical formulation is selected from the group consisting of tablets, capsules, caplets, solutions, suspensions syrups granules, beads, powders and pellets.

Claim 13 (Original). The method of claim 12, wherein the pharmaceutical formulation comprises a tablet.

Claim 14 (Original). The method of claim 12, wherein the pharmaceutical formulation comprises a capsule.

Claim 15 (Currently amended). The method of claim 1, wherein the [active agent] antidepressant drug is administered transmucosally.

Claim 16 (Currently amended). The method of claim 15, wherein the [active agent] antidepressant drug is administered sublingually.

Claim 17 (Currently amended). The method of claim 15, wherein the [active agent] antidepressant drug is administered buccally.

Claim 18 (Currently amended). The method of claim 15, wherein the [active agent] antidepressant drug is administered intranasally.

Claim 19 (Currently amended). The method of claim 15, wherein the [active agent] antidepressant drug is administered transurethrally.

Claim 20 (Currently amended). The method of claim 15, wherein the [active agent] antidepressant drug is administered rectally.

Claim 21 (Currently amended). The method of claim 1, wherein the [active agent] antidepressant drug is administered by inhalation.

Claim 22 (Currently amended). The method of claim 1, wherein the [active agent] antidepressant drug is administered transdermally.

Claim 23 (Original). The method of claim 1, wherein the active agent is administered parenterally.

Claim 24 (Original). The method of claim 1, wherein the antidepressant drug is selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressant drugs, and combinations thereof.

Claim 25 (Currently amended). The method of claim 24, wherein the antidepressant drug is selected from the group consisting of amitryptiline, amoxapine, butriptyline, [clomipramine,] demexiptiline, desipramine, dibenzepin, dimetacrine, dothiepin, doxepin, imipramine, iprindole, lofepramine, maprotiline, melitracen, metapramine, mianserin, mirtazapine, nortryptiline,

propizepine, protriptyline, quinupramine, setiptiline, tianeptine, trimipramine, and combinations thereof.

Claims 26-27 (Currently canceled).

Claim 28 (Currently amended). The method of claim 1, wherein the antidepressant drug is [selected from the group consisting of] a monoamine oxidase [inhibitors] inhibitor.

Claim 29 (Currently amended). The method of claim 28, wherein the [antidepressant drug] monoamine oxidase inhibitor is selected from the group consisting of amiflamine, brofaromine, clorgyline, α-ethyltryptamine, iproclozide, iproniazid, isocarboxazid, mebanazine, moclobemide, nialamide, pargyline, phenelzine, pheniprazine, pirlindole, safrazine, selegiline, toloxatone, tranylcypromine, and combinations thereof.

Claim 30 (Currently amended). The method of claim 1, wherein the antidepressant drug is [selected from the group consisting of] an azaspirone [antidepressants] antidepressant.

Claim 31 (Currently amended). The method of claim 30, wherein the azaspirone antidepressant [drug] is selected from the group consisting of buspirone, gepirone, ipsapirone, tandospirone, tiaspirone, and combinations thereof.

Claim 32 (Currently amended). The method of claim 1, wherein the antidepressant drug is an atypical non-SRI antidepressant selected from the group consisting of amesergide, amineptine, benactyzine, bupropion, fezolamine, levoprotiline, medifoxamine, mianserin, minaprine, oxaflozane, oxitriptan, rolipram, teniloxazine, tofenacin, trazodone, tryptophan, viloxazine, and combinations thereof.

Claim 33 (Original). The method of claim 1, further comprising administering at least one additional active agent with the antidepressant drug.

Claim 34 (Original). The method of claim 33, wherein the additional active agent is a vasoactive agent selected from the group consisting of nitroglycerin, isosorbide dinitrate, erythrityl tetranitrate, amyl nitrate, sodium nitroprusside, molsidomine, linsidomine chlorhydrate, S-nitroso-N-acetyl-d,l-penicillamine, S-nitroso-N-cysteine and S-nitroso-N-glutathione, diazenium diolates ("NONOates"), phenoxybenzamine, dibenamine, doxazosin, terazosin, phentolamine, tolazoline, prazosin, trimazosin, alfuzosin, tamsulosin, indoramin, ergotamine, acetergamine, brazergoline, bromerguride, cianergoline, delorgotrile, disulergine, ergonovine maleate, ergotamine tartrate, etisulergine, lergotrile, lysergide, mesulergine, metergoline, metergotamine, nicergoline, pergolide, propisergide, proterguride, diazoxide, hydralazine, minoxidil nimodepine, pinacidil, cyclandelate, dipyridamole, isoxsuprine, chlorpromazine, haloperidol, yohimbine, prostaglandin E_0, prostaglandin E_1, prostaglandin A_1, prostaglandin B_1, prostaglandin $F_{1\alpha}$, 19-hydroxy- prostaglandin A_1, 19-hydroxy- prostaglandin B_1, prostaglandin E_2, prostaglandin A_2, prostaglandin B_2, 19-hydroxy- prostaglandin A_2, 19-hydroxy- prostaglandin B_2, prostaglandin E_3, prostaglandin $F_{3\alpha}$, carboprost tromethamine, dinoprost tromethamine, dinoprostone, lipoprost, gemeprost, metenoprost, sulprostone, tiaprost, vasoactive intestinal peptide, and combinations thereof.

Claim 35 (Original). The method of claim 33, wherein the additional active agent is a phosphodiesterase inhibitor.

Claim 36 (Original). The method of claim 35, wherein the phosphodiesterase inhibitor is a Type III, Type IV, Type V, or nonspecific phosphodiesterase inhibitor.

Claim 37 (Original). The method of claim 33, wherein the additional active agent is selected form the group consisting of cianopramine, citalopram, femoxetine, fluoxetine, fluvoxamine, ifoxetine, milnacipran, nomifensine, oxaprotiline, paroxetine, sertraline, sibutramine, venlafaxine, viqualine, zimeldine, clovoxamine, etoperidone, methylphenidate, nefazodone, opipramol, 2-methyl serotonin, lysergic acid diethylamide, ergot alkaloids, 8-hydroxy-(2-N,N-dipropylamino)-tetraline, 1-(4-bromo-2,5-dimethoxyphenyl)-2-aminopropane, cisapride, sumatriptan, *m*-chlorophenylpiperazine, zacopride, mezacopride, ondansetron, granisetron,

metoclopramide, tropisetron, dolasetron, trimethobenzamide, methysergide, risperidone, ketanserin, ritanserin, clozapine, R(+)- -(2,3-dimethoxyphenyl)-1-[2-(4-fluorophenyl)ethyl]-4-piperidine-methanol, azatadine, cyproheptadine, fenclonine, dexfenfluramine, fenfluramine, chlorpromazine, methoxamine, methpentermine, metaraminol, mitodrine, clonidine, apraclonidine, guanfacine, guanabenz, methyldopa, amphetamine, methamphetamine, epinephrine, norepinephrine, ethylnorepinephrine, phenylephrine, ephedrine, pseudoephedrine, pemoline, naphazoline, tetrahydrozoline, oxymetazoline, xylometazoline, phenylpropanolamine, phenylethylamine, dopamine, dobutamine, colterol, isoproterenol, isotharine, metaproterenol, terbutaline, tyramine, hydroxyamphetamine, ritodrine, prenalterol, albuterol, isoetharine, pirbuterol, bitolterol, fenoterol, formoterol, procaterol, salmeterol, mephenterine, propylhexedrine, phenoxybenzamine, phentolamine, tolazoline, prazosin, terazosin, doxazosin, trimazosin, yohimbine, labetalol, urapidil, alfuzosin, bunazosin, tamsulosin, haloperidol, phenothiazines, butyrophenones, propranolol, nadolol, timolol, pindolol, metoprolol, atenolol, esmolol, acebutolol, bopindolol, carteolol, oxprenolol, penbutolol, carvedilol, medroxalol, naftopidil, bucindolol, levobunolol, metipranolol, bisoprolol, nebivolol, betaxolol, carteolol, celiprolol, sotalol, propafenone, indoramin, bethanidine, debrisoquine, guabenxan, guanadrel, guanazodine, guanethidine, guanoclor, guanoxan, alprazolam, brotizolam, chlordiazepoxide, clobazepam, clonazepam, clorazepate, demoxepam, diazepam, estazolam, flurazepam, halazepam, lorazepam, midazolam, nitrazepam, nordazapam, oxazepam, prazepam, quazepam, temazepam, triazolam, pharmacologically acceptable salts thereof, and combinations of any of the foregoing.

Claim 38 (Original). The method of claim 37, wherein the additional active agent is selected from the group consisting of alprazolam, brotizolam, chlordiazepoxide, clobazepam, clonazepam, clorazepate, demoxepam, diazepam, estazolam, flurazepam, halazepam, lorazepam, midazolam, nitrazepam, nordazapam, oxazepam, prazepam, quazepam, temazepam, triazolam, and pharmaceutically acceptable salts thereof.

Claim 39 (Original). The method of claim 37, wherein the additional active agent is selected from the group consisting of fluoxetine, fluvoxamine, paroxetine, sertraline, and pharmaceutically acceptable salts thereof.

Claim 40 (Currently amended). A pharmaceutical formulation for treating premature ejaculation, comprising a rapid-release [rapid release] formulation of a therapeutically effective amount of an antidepressant drug selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressants, MAO inhibitors, azaspirone antidepressants, and atypical non-SRI antidepressants, in an amount effective to delay the onset of ejaculation by the individual during sexual activity, and a pharmaceutically acceptable carrier, wherein the formulation releases the drug at a rate effective to provide a systemically effective level of the drug within 3.5 hours of administration to a patient.

Claim 41 (Original). The formulation of claim 40, wherein the antidepressant drug is selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressant drugs, and combinations thereof.

Claim 42 (Currently Amended). The formulation of claim 41, wherein the antidepressant drug is selected from the group consisting of amitryptiline, amoxapine, butriptyline, [clomipramine,] demexiptiline, desipramine, dibenzepin, dimetacrine, dothiepin, doxepin, imipramine, iprindole, lofepramine, maprotiline, melitracen, metapramine, mianserin, mirtazapine, nortryptiline, propizepine, protriptyline, quinupramine, setiptiline, tianeptine, trimipramine, and combinations thereof.

Claims 43-44 (Currently canceled).

Claim 45 (Original). The formulation of claim 40, wherein the antidepressant drug is selected from the group consisting of monoamine oxidase inhibitors.

Claim 46 (Original). The formulation of claim 45, wherein the antidepressant drug is selected from the group consisting of amiflamine, brofaromine, clorgyline, α-ethyltryptamine, iproclozide, iproniazid, isocarboxazid, mebanazine, moclobemide, nialamide, pargyline, phenelzine, pheniprazine, pirlindole, safrazine, selegiline, toloxatone, tranylcypromine, and combinations thereof.

Claim 47 (Original). The formulation of claim 40, wherein the antidepressant drug is selected from the group consisting of azaspirone antidepressants.

Claim 48 (Original). The formulation of claim 47, wherein the antidepressant drug is selected from the group consisting of buspirone, gepirone, ipsapirone, tandospirone, tiaspirone, and combinations thereof.

Claim 49 (Original). The formulation of claim 40, wherein the antidepressant drug is an atypical non-SRI antidepressant selected from the group consisting of amesergide, amineptine, benactyzine, bupropion, fezolamine, levoprotiline, medifoxamine, mianserin, minaprine, oxaflozane, oxitriptan, rolipram, teniloxazine, tofenacin, trazodone, tryptophan, viloxazine, and combinations thereof.

Claim 50 (Original). The formulation of claim 40, in unit dosage form.

Claim 51 (Original). The formulation of claim 50, wherein the antidepressant drug is present in an amount of about 0.1 mg to about to about 300 mg.

Claim 52 (Currently amended). The formulation of claim 51, wherein the amount is in the range of about 1 mg to about <u>100 mg</u> [100mg].

Claim 53 (Original). The formulation of claim 52, wherein the amount is in the range of about 1 mg to about 50 mg.

Claim 54 (Original). The formulation of claim 40, in the form of a rapidly disintegrating tablet.

Claim 55 (Original). The formulation of claim 40, in the form of an effervescent tablet.

Claim 56 (Original). The formulation of claim 40, in the form of an open matrix network tablet.

Claim 57 (Original). A formulation of claim 40, adapted for transmucosal drug administration, wherein the carrier is suitable for transmucosal drug delivery buccally, sublingually, intranasally, rectally, or by inhalation.

Claim 58 (Original). The formulation of claim 57, comprising a solid dosage form for application to the buccal mucosa, and wherein the carrier is suitable for buccal drug delivery.

Claim 59 (Original). The formulation of claim 58, wherein the carrier is a hydrolyzable polymer.

Claim 60 (Original). The formulation of claim 59, wherein the dosage form further comprises an adhesive suitable for affixing the dosage form to the buccal mucosa.

Claim 61 (Original). The formulation of claim 57, comprising a dosage form for application to the sublingual mucosa, and wherein the carrier is suitable for sublingual drug delivery.

Claim 62 (Original). The formulation of claim 57, comprising a dosage form for application to the rectal mucosa, and the carrier is suitable for rectal drug delivery.

Claim 63 (Original). The formulation of claim 62, comprising a rectal suppository.

Claim 64 (Original). The formulation of claim 57, comprising a dosage form suitable for inhalation.

Claim 65 (Original). The formulation of claim 64, comprising a liquid.

Claim 66 (Original). The formulation of claim 64, comprising a dry powder.

Claim 67 (Original). The formulation of claim 64, comprising an aerosol composition.

Claim 68 (Original). The pharmaceutical formulation of claim 40, comprising an intranasal solution.

Claim 69 (Original). The formulation of claim 40, in the form of a gum.

Claim 70 (Original). The formulation of claim 40, in the form of a transdermal drug delivery device adapted to be affixed to an individual's body surface.

Claim 71 (Currently amended). A packaged kit for a patient to use in the treatment of premature ejaculation, comprising: a rapid-release pharmaceutical formulation of an antidepressant drug selected from the group consisting of tricyclic antidepressants, tetracyclic antidepressants, MAO inhibitors, azaspirone antidepressants, and atypical non-SRI antidepressants, wherein the formulation releases the drug at a rate effective to provide a systemically effective level of the drug within 3.5 hours of administration to a patient; a container housing the pharmaceutical formulation during storage and prior to administration; and instructions for carrying out drug administration in a manner effective to treat premature ejaculation.

Claim 72 (Original). The packaged kit of claim 71, wherein the pharmaceutical formulation is a rapid-release dosage form containing a unit dosage of the antidepressant drug, the unit dosage being a therapeutically effective dosage for treatment of premature ejaculation.

REMARKS

Claims 1-72 are pending. Claims 1, 4-7, 11, 15-22, 25, 28-32, 40, 42, 52 and 71 are amended. Claims 2-3, 8-10, 12-14, 23-24, 33-39, 41, 45-51, 53-70, and 72 remain unchanged. Claims 26-27 and 43-44 are canceled.

Claims 1-11, 15, 24-26, 28-32, 40-43, 45-50, 71 and 72 are rejected. Claims 12-14, 16-23, 27, 33-39, 44, and 51-70 are objected to as being dependent upon a rejected base claim.

THE AMENDMENT

Claim 1 has been amended to recite that the formulation is administered systemically, support for which may be found, for example, at page 5, lines 11-12 of the Specification. Claim 1 has been amended to recite that the formulation is administered less than 3.5 hours prior to anticipated sexual activity, support for which may be found, for example, on page 6, lines 17-19; page 9, lines 14-26, and page 24, lines 22-24 of the Specification. Support for "anticipated sexual activity" can be found, for example, at page 5, lines 6-8 of the Specification. Claim 1 has also been amended to recite that the formulation is rapid-release, support for which may be found, for example, at page 18, line 4 of the Specification. Claim 1 has been amended to recite that a systemically effective level of the active agent is achieved within 3.5 hours of administration, support for which may found, for example, at page 18, lines 4-8 of the Specification. Support for the aforementioned language can also be found in the parent application, U.S. Patent Application Serial No. 09/721,412, the disclosure of which was incorporated by reference at page 1, lines 7-9 of the Specification.

Claims 40 and 71 have been amended to recite systemically effective levels within 3.5 hours of administration, and claim 71 has been amended to recite a "rapid-release" formulation.

Claim 40 has been amended to recite drug administration effective to delay the onset of ejaculation during sexual activity, support for which can be found, for example, at page 5, lines 27-28 of the Specification.

Claims 25 and 42 have been amended to delete the term "clomipramine," which has necessitated the cancellation of Claims 26-27 and 43-44.

Claims 4-5, 11, 15-22, 28-32, and 52 have been amended to correct informalities such as typographical errors, corrections to claim dependencies and to recite consistent language.

Neither the cancellation of claims nor the amendment of pending claims should be construed as abandonment of any canceled subject matter.

No new matter has been added.

OBJECTION UNDER 37 C.F.R. §1.75(c)

Claim 8 has been objected to under 37 C.F.R. §1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. In particular, the Examiner asserts that Claim 8 fails to further limit the prior claims since treatment is directed to premature ejaculation during sexual intercourse. The Examiner argues that no other sexual activity is disclosed or suggested. While the Examiner is correct that sexual intercourse is the only sexual activity specifically stated in the specification, that was merely listed as an exemplary sexual activity and the invention is not limited to such.

Applicants assert that one skilled in the art, e.g., a physician treating patients suffering from a sexual dysfunction, would understand that the term "sexual activity" encompasses numerous activities other than sexual intercourse. For example, masturbation would be one such activity that is also clearly understood to be a "sexual activity". More importantly, premature ejaculation, to which the instant invention is addressed, may well be of concern to participants of that activity.

Finally, the term "sexual activity" as used in the patent literature also has a breadth of meaning. See for example, U.S. Patent No. 6,455,564 to Meglasson et al., where the term "sexual activity" is recited in claims directed at treating male erectile disorder. The term is noted in the specification to include "sexual intercourse with or without orgasm, ejaculation, masturbation and sexual foreplay".

In conclusion, Applicants are entitled to the broadest interpretation of the claim language which this specification will support. The specification clearly intended to include other activities within the meaning of the term "sexual activity" because the specification recites that "The terms "treating" and "treatment" as used herein refer to the ability to increase an individual's ejaculatory latency (i.e., delay ejaculation) during sexual activity, particularly sexual intercourse,..." [emphasis added]. This, in combination with other patent language and the

knowledge of those skilled in the art, indicates that Claim 8 is proper. Applicants respectfully request withdrawal of the rejection.

REJECTION UNDER 35 U.S.C. §102(b) OVER ROWLAND

Claims 1-11, 24-26 and 40-43 stand rejected under 35 U.S.C. §102(b) as being anticipated by Rowland et al. (1998) *Drugs of Today* 34(10):879-899 (hereinafter "Rowland").

Rowland is cited as disclosing the treatment of premature ejaculation by administration of clomipramine, administered less than one hour prior to ejaculation (Results/effectiveness heading for all clomipramine studies). The Examiner notes that administration may occur at much as 4-6 hours prior (page 892, lines 1-2). The Examiner also notes that while Rowland does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention.

Claim 1, as amended recites a method for treating premature ejaculation by "systemically" administering a "rapid-release" pharmaceutical formulation containing an antidepressant "less than 3.5 hours prior to anticipated sexual activity", wherein the formulation releases the drug at a rate that provides a "systemically effective level of the drug within 3.5 hours of administration." Claim 40, as amended, recites a pharmaceutical formulation for treating premature ejaculation, comprising a rapid-release formulation of an antidepressant drug "in an amount effective to delay the onset of ejaculation by the individual during sexual activity" and provides a "systemically effective level of the drug within 3.5 hours of administration."

The Examiner has interpreted the reference as disclosing administration of clomipramine less than an hour prior to ejaculation, citing the table on pages 890-891. Applicants respectfully disagree with the Examiner's interpretation of the reference, for the following reasons. Rowland et al., on page 889, second column, under the heading "1) Tricyclic antidepressants (Table I)," discloses administration of clomipramine in three different ways:

(1) chronically, at 25 mg/day or 50 mg/day;

(2) on an as-needed basis 12-24 hours prior to anticipated intercourse; and

(3) on an as-needed basis 4-6 hours prior to intercourse.

There is no teaching or suggestion of administering clomipramine less than 3.5 hours prior to anticipated sexual activity (Claim 1) or in an amount effective to delay the onset of

ejaculation by the individual during sexual activity (Claim 40). With respect to the entries in Table I pertaining to clomipramine, the data in the right-hand column (entitled "Results/effectiveness") pertains to "ejaculatory latency," which the authors define in the conventional sense to mean the time period between vaginal intromission and ejaculation (see page 881 of the reference, under "Latency to ejaculation"). Ejaculatory latency does not refer to the time period between drug administration and ejaculation. See, for example, the data on page 890 relating to a study by Althof et al. In that study, as may be seen under the column "Dose/frequency," clomipramine was given 25 mg/day or 50 mg/day, on an ongoing (chronic) basis. The table indicates, in the right-hand column, that those patients receiving 25 mg/day experienced an increase in ejaculatory latency from a baseline of 81 seconds to 202 seconds, while patients receiving 50 mg/day experienced an increase in ejaculatory latency from a baseline of 81 seconds to 419 seconds. There is no indication, in the table, that clomipramine was ever administered less than 4 hours prior to sexual activity. Any references in the Rowland table to administration of drugs at 30 minutes or 1 hour before coitus, refer to lidocaine/prolacaine and S-S cream, respectively, cream formulations of drugs that are unrelated to the methods and formulations presently claimed.

As noted above, the Examiner indicates that while Rowland does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention. However, anticipation of a claimed invention by a prior art reference under 35 U.S.C. §102(b) requires the presence in a single prior art reference of each and every element of a claimed invention. The "rapid-release" aspect of the claimed invention is related to the recitation of administration less than 3.5 hours prior to anticipated sexual activity, as well as the formulation providing a systemically effective level of the drug within 3.5 hours of administration. Rowland does not teach or even suggest a rapid-release formulation and does not teach a dosing regimen that would suggest the desirability of a rapid-release formulation. There mere fact that Rowland does not teach away from a rapid-release formulation does not constitute anticipation.

Applicants' claimed method and formulation relate to an as-needed basis administration, with "as-needed basis" defined in the specification to mean that the method does not involve chronic pharmacotherapy. Rather, administration is on an as-needed basis, which involves

administration shortly before anticipated sexual activity (page 5, lines 6-8 of the specification). This typically includes administration immediately prior to sexual activity (page 9, line 21); up to about 2 or 3 hours prior to anticipated sexual activity (page 6, lines 17-19); about 0.25 to 3.5 hours, about 0.5 to 3 hours, or about 1 to 2.5 hours prior to anticipated sexual activity (page 9, lines 21-23); or within a 0.25 to 3-hour window prior to anticipated sexual activity (page 24, lines 23-24). Claim 1 has been amended to includes these ranges in the recitation of "less than 3.5 hours."

Accordingly, Applicants are not acquiescing in the rejection but have nevertheless amended Claims 1 and 40 to clarify the recited method and formulation relative to the disclosure of Rowland. Claim 1 now specifies that that the formulation is administered less than 3.5 hours prior to engaging in sexual activity, and Claims 1 and 40 have both been amended to recite that the formulation is rapid-release and that the drug is released to provide a systemically effective level of drug within 3.5 hours of administration. Since the absolute minimum time period disclosed by Rowland is 4 hours prior to sexual activity, with "as needed" administration actually defined as 12-24 hours prior to sexual activity (see page 889, right-hand column), the presently amended claims 1 and 40 are clearly distinguished over the reference.

Accordingly, since Rowland does not teach, or even suggest the invention as presently claimed, Applicants assert that the invention is patentable under 35 U.S.C. §102(b).

REJECTION UNDER 35 U.S.C. §102(b) OVER SMITH

Claims 1-11, 15, 24-26, 28-32, 40-43 and 45-50 stand rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,922,341 to Smith et al. (hereinafter "Smith").

Smith is cited as disclosing a method for delaying the onset of ejaculation through the use of various compounds (Abstract), including antidepressants (col. 3, lines 20-25) such as clomipramine (col. 5, line 12). The Examiner also notes that while Smith does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention.

As noted above, Claim 1, as amended recites a method for treating premature ejaculation by systemically administering a rapid-release formulation less than 3.5 hours prior to anticipated sexual activity, and the formulation releases drug at a rate that provides systemically effective

levels of drug within 3.5 hours of administration. Claim 40, as amended, recites a pharmaceutical formulation for treating premature ejaculation, comprising a rapid-release formulation in an amount effective to delay the onset of ejaculation during sexual activity and that releases drug at a rate effective to provide systemically effective levels of drug within 3.5 hours of administration.

Therefore, the invention as presently claimed relates to systemic administration. Systemic administration is to be contrasted with local administration, which is the primary focus of the Smith reference. Local administration would not be expected to provide "systemically effective" levels of an active agent as is required by Applicants' claimed invention. Also, although Smith states that "with some active agents, [administration can be] just prior to intercourse" (column 12, lines 7-8), Smith does not teach or suggest drug administration less than 3.5 hours prior to sexual activity and/or systemic levels achieved within 3.5 hours of administration, as is required by the amended claims.

In addition, contrary to the Examiner's assertion, Smith does not explicitly describe oral or transmucosal administration of an active agent. Col. 9, lines 39-56 of Smith describes transurethral delivery as well as other types of local delivery and mentions intracavernosal injection, topical application and transdermal application. This section of Smith also mentions that "depending on the intended mode of administration, the pharmaceutical compositions may be in the form of solid, semi-solid or liquid dosage forms, such as, for example, tablets, suppositories, pills, capsules, powders, liquids, suspensions, creams, ointments, lotions or the like, preferably in unit dosage form suitable for single administration of a precise dosage". Although various dosage forms are described in this section of the Smith specification, it is made clear throughout the Smith patent that drug administration is intended to be local, and that such local delivery contrasts with oral, systemic administration. See the discussion in the Background section of Smith, regarding the distinctions between oral, systemic delivery and local administration, that latter being the focus of the Smith invention. Also see col. 12, lines 16-19, where Smith states that "[b]y administering the drug locally, the side effects, drug interactions and disease considerations of systemic (e.g., oral) drug administration are avoided." Applicants assert that this statement evidences that Smith actually teaches away from systemic methods and compositions, as are presently claimed.

Finally, as noted above, the Examiner indicates that while Smith does not describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention. As Applicants argued above with regard to the Rowland reference, anticipation requires the presence in a single prior art reference of each and every element of a claimed invention. Smith does not teach or even suggest a rapid-release formulation and does not teach a dosing regimen that would suggest the desirability of a rapid-release formulation. There mere fact that Smith does not teach away from a rapid-release formulation does not constitute anticipation.

Accordingly, since the Smith reference does not teach, or even suggest the invention as presently claimed, Applicants assert that the invention is patentable under 35 U.S.C. §102(b).

REJECTION UNDER 35 U.S.C. §103(a), OVER ROWLAND OR SMITH

Claims 71-72 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Rowland or Smith.

Rowland is cited as disclosing the treatment of premature ejaculation by administration of clomipramine, administered less than one hour prior to ejaculation. Smith is cited as disclosing a method for delaying the onset of ejaculation through the use of various compounds, including antidepressants such as clomipramine. The Examiner also notes that while neither Rowland or Smith describe a rapid-release dosage, no mention is made of sustained or extended release that would teach away from the instant invention. The Examiner also notes that neither reference mentions packaging the composition in a kit, but relies on the knowledge in the art that pharmaceuticals are routinely packaged in kits.

Claim 71, as amended, recites a packaged kit for a patient to use in the treatment of premature ejaculation, comprising a rapid-release pharmaceutical formulation that releases the drug at a rate effective to provide a systemically effective level of the drug within 3.5 hours of administration to a patient.

For the reasons set forth above, Rowland and Smith do not teach or suggest a ***rapid-release*** formulation that provides ***systemic*** delivery within 3.5 hours of administration to a patient. Therefore, even assuming for arguments sake that pharmaceuticals are routinely packaged in kits, one of skill in the art would still not arrive at Applicants' claimed invention

after reviewing the Rowland or the Smith reference since they do not teach or suggest the rapid-release and systemic features of the claimed invention.

OTHER REFERENCES NOTED

Girgis et al. (1982) *Andrologia* 14(4):364-368 and Assalian (1988) *The Journal of Sex Research* 24:213-215 are cited for their equivalent teaching of the use of clomipramine in the treatment of premature ejaculation. However, they do not form the basis of a rejection under 35 U.S.C. §102 or §103.

Applicants have reviewed these references and agree with the Examiner's implicit finding that the references do not disclose or suggest, either individually or in combination, the presently claimed invention.

SUMMARY

The above arguments and amendments to the Claims are submitted for the purpose of facilitating allowance of the Claims and a sincere effort has been made to place this application in condition for allowance. An early notice of allowance is earnestly requested.

If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (650) 330-4916.

Respectfully submitted,

By: Shelley P. Eberle
Shelley P. Eberle
Registration No. 31,411

REED & EBERLE LLP
800 Menlo Avenue, Suite 210
Menlo Park, California 94025
(650) 330-0900 Telephone
(650) 330-0980 Facsimile

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